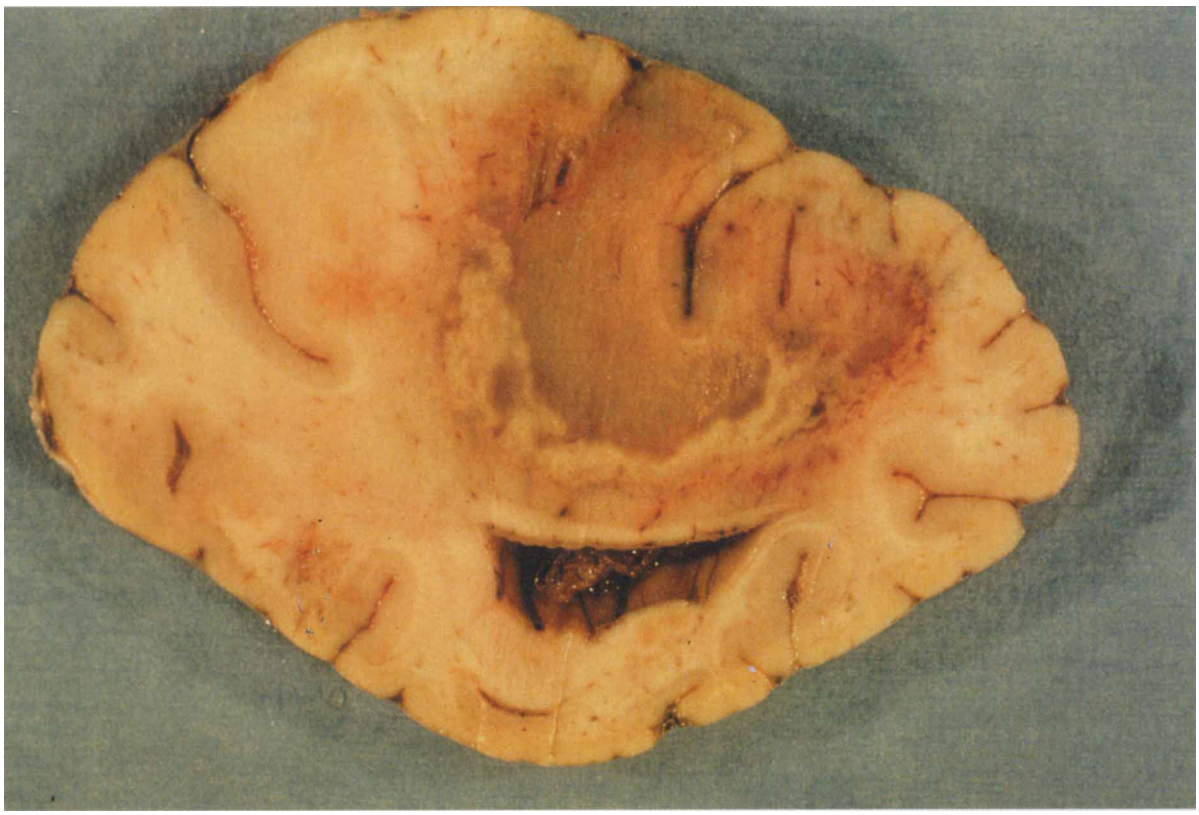
Illustrated continuing medical education



A 29-year-old student from El Salvador, who was known to be HIV positive, presented to Accident and Emergency department having had a generalised seizure. Over the previous 10 days a colleague had noticed increasingly bizarre behaviour in that he had been unable to recognise friends and relatives, and had complained of headaches, flashing lights and nausea. On examination he had severe oropharyngeal candidiasis and was disorientated in time, person and place. He had a right total homonymous hemianopia and visual inattention on the right side. There was no meningism. Initial tests revealed normal FBC, U&E, LFT's with negative toxoplasma and syphilis serology and negative cryptococcal antigen. CMV IgG was detected, but CMV Direct Antigen Test was negative. MRI scan showed multiple ring-enhancing lesions, the largest in the left occipital lobe.

Questions

1. What is the differential diagnosis
2. Which test result is unexpected
3. What initial treatment is indicated
4. What is the prognosis

Answers

1. Cerebral *Toxoplasma gondii*, primary CNS lymphoma and progressive multifocal leukoencephalopathy (PML) together account for 80%–90% of focal neurological lesions. Less commonly mass lesions can be caused by *Cryptococcus neoformans*, pyogenic or tuberculous abscesses, and more rarely *Nocardia asteroides*, *Treponema pallidum*, cytomegalovirus (CMV), *Candida albicans* and *Histoplasma capsulatum*.
2. The toxoplasma serology. Despite negative serology (serology is negative in 3–5% of cases of toxoplasmic encephalitis), toxoplasmosis is still the most likely diagnosis.
3. Pyrimethamine (200 mg loading dose, followed by 50–75 mg/day oral) and sulfadiazine (4–6 g 6 h oral or intravenous), with folinic acid (15–20 mg/day, oral). Clindamycin may replace sulfadiazine if intolerance occurs of the latter.
4. If patients are going to respond they tend to in 3 (50%) to 7 (90%) days. Early mortality is as high as 16%, and 40–50% will have residual neurological impairment. Without secondary prophylaxis reactivation occurs in up to 80% of patients. Median survival after infection has been reported in the range of 224 to 490 days.

Neurological disorders cause considerable morbidity and mortality in patients with AIDS. At least 40% of HIV-infected patients develop neurological symptoms during the course of their illness. With suspected toxoplasmosis most centres recommend a therapeutic trial of antimicrobials for 10–14 days, with brain biopsy being reserved for non-responders or those deteriorating on therapy. Factors reported to be associated with poorer outcome include fever greater than 38.4°C, depression of conscious level at presentation, presence of multiple lesions on neuroimaging studies, previous opportunistic infections and the use of anticonvulsants. Cerebrospinal fluid (CSF) analysis generally adds little diagnostic information in such patients. The fluid may be normal or have mild pleocytosis and elevated protein levels. Only 30–50% of patients have demonstrable anti-toxoplasma antibodies in the CSF. Newer diagnostic techniques include PCR for *T gondii* DNA in the CSF (sensitivity 50–76%; specificity 100%) and functional imaging techniques e.g. SPECT (single-photon emission computed tomography) and PET (positron emission tomography). These studies rely on rapidly dividing and growing cells taking up more radiolabelled substrate than inflammatory lesions, and are therefore useful in differentiating lymphoma from infections such as toxoplasmosis.

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